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David G. Kent

Perhaps the most compelling experiment was a head-to-head comparison of CD34⁺ cells treated for 8 hours with NOV or not. Following rigorous limiting dilution primary and secondary transplantation experiments in mice, it was clear that the NOV-treated cells were superior in their ability to perform as functional stem cells in transplantation. Importantly, no cells divide in this

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short 8-hour culture, thereby excluding in vitro HSC expansion as a mechanism. This latter point was supported by in vitro single cell assays and the paper ends up concluding that coaxing cells to be in the correct “state” for subsequent engraftment could be achieved.

Previous studies have hinted that cell cycle regulation and “quiescence exit” in particular would be critical to our ability to manipulate how blood stem cells are called into action. CDK6 levels were identified by the Dick⁵ and Sexl groups⁶ in 2015 as a key regulator of quiescence exit and understanding its molecular mechanism would help determine the speed at which a blood stem cell could leave its hibernating state. Other studies have focused on the initial harvest of cord blood from donors. Of interest here is the work of Mantel/O’Leary et al⁷ who showed that reducing the loss of stem cells in a cord blood harvest could be achieved by not exposing them to extra-physiological oxygen levels.

Together, these multiple lines of evidence suggest that the potential for large numbers of stem cells exist in a single cord and it is down to the research community to identify the best method of preserving and/or activating them to be most productive in a

post-transplantation scenario where they must seed the production of blood cells for the remainder of the patient’s lifetime.

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